Foreign Agricultural Service
GAIN Report
Global Agriculture Information Network

Voluntary Report - public distribution

Date: 12/19/2001

GAIN Report #TW1052

Taiwan

Biotechnology

Safety Assessment Guidelines for Biotech Foods

2001

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Report Highlights:
The Department of Health (DOH) released the official English language guidelines for safety assessment of genetically modified foods as well as safety assessment procedures. To date, only one company has filed registration applications for one bioengineered soybean and one Bt corn variety. DOH urges biotechnology companies to register bioengineered corn and soybean varieties currently exported to Taiwan by DOH's April 30, 2002 submission deadline. Beginning January 1, 2003, only raw commodities or foods produced from approved bioengineered soybean and corn varieties will be eligible for commercialization on Taiwan.

Includes PSD changes: No
Includes Trade Matrix: No
Unscheduled Report
Taiwan [TW1], TW

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Registration of Bioengineered Varieties

The Food Sanitation Bureau (FSB) of the Department of Health (DOH) recently released the official English language "Guidance for Safety Assessment for Genetically Modified Foods." The full text of the guidance is reproduced below. The information will be available online shortly at the DOH website: http://www.doh.gov.tw/english/food/

The current Taiwan bioengineered food regulations focus on corn and soybeans and products made from corn and soybeans. DOH urges agricultural biotechnology companies to register all bioengineered varieties of soybeans and corn marketed on Taiwan prior to April 30, 2002. The mandatory bioengineered food labeling regulation will take effect on January 1, 2003. As of that date, bioengineered soybean and corn foods are eligible for commercialization, only if they are registered with the DOH.

According to DOH, the one bioengineered soybean and six bioengineered corn varieties are currently being imported and are expected to be registered. DOH bases its assumptions on product registrations in other markets, not on testing of shipments to Taiwan. To date, only two registration packages, one for Glyphosate tolerant soybean and one for Bt corn, have been submitted. DOH expects an additional five corn varieties to be registered - two Glyphosate tolerant and three Glufosinate tolerant.

According to information post has received, the data and information requested in the registration package is the same as the U.S. Food and Drug Administration package. However, the information is presented in a different order. Working closely with DOH, the registrant can lessen the effort required to reorder the package.

DOH established the Genetically Modified Foods Advisory Committee (GMFAC) to undertake safety assessments using the published guidance (the Chinese language version has been out since February 2001). DOH will most likely certify a GM variety for a period not to exceed five years. Application for renewal must be filed three months prior to the expiration term.

Registration Package:

As reported in TW1007, the applicant is required to fill out the official application form, available on the DOH website, and provide the following information:

(1) Background information about the applicant.
(2) Background information about the GM food.
(3) Synopsis of the safety assessment on the GM food.
(4) Safety assessment on the GM food.
(5) A literature list of references and relevant research papers on the GM food.
(6) Reference sample and registration fee.

Registration requires one kilogram of sample. The registration fee is NT$164,000 or about $4,754 per variety ($1=NT$34.5 quoted 12/18/01). This includes NT$100,000 for documentation review and evaluation and NT$64,000 for testing the validity of variety identification method(s). The DOH's National Laboratories of Foods and Drugs (NLFD) will conduct the testing.

Registration/Safety Assessment Procedures:

(1) Submission of application to DOH--The applicant sends in the application dossier and application fee (NT$100,000 in cash or check) to DOH.
(2) DOH Notification--DOH notifies the applicant to submit reference sample to NLFD.
(3) DOH Notification--DOH notifies NLFD the submission case.
(4) Submission of reference sample to NLFD--The applicant brings with the DOH notification letter, reference sample (properly sealed), document describing method of detection and examination fee (NT$64,000 in cash or check) to NLFD.
(5) Genetically Modified Foods Advisory Committee (GMFAC) Assessment-- After reviewing the case, DOH calls for GMFAC meetings to evaluate the application according to the Guidance of Safety Assessment for Genetically Modified Foods (see the text section).
(6) GMFAC Report-- After completion of evaluation, GMFAC sends assessment report and recommendation to DOH.
(7) Examination report-- NLFD notifies DOH the result of examination.
(8) Completion of Registration Upon acceptance–DOH issues the applicant a certificate according to NLFD examination report and GMFAC assessment report.

Contact information for registration of bioengineered varieties

DOH Contact Point	NLFD Contact Point
Shu-Kong Chen, Director Food Sanitation Bureau Department of Health 12 floor, 100 Ai-Kuo E. rd., Taipei 100, Taiwan phone: 886-2-2321-0151 ext. 341 fax: 886-2-2392-9723 or 886-2-2358-2433 e-mail: fscskg@doh.gov.tw Web: http://www.doh.gov.tw/english/food/	Yang-chih Shih, Director Division of Food Mirobiology 161-2 Kuen-Yang Street Nankang, Taipei 115 Taiwan, ROC phone: 886-2-2653-1265 fax: 886-2-2653-1268 e-mail:shihdyc@nlfd.gov.tw Web: http://www.nlfd.gov.tw

Text: The Guidance of Safety Assessment for Genetically Modified Foods
(Version 5.1, Last updated 12/14/2001 Department of Health)

Begin text:

Chapter One: General Provisions

I. Basis of the rule

This guidance is prescribed in accordance with the provision of paragraph 1 of Article 14 of the Law Governing Food Sanitation.

II. Objective

This guidance explains the information required for safety assessment of genetically modified foods (hereafter as GM foods). The original developers are required to submit necessary information to register their GMO to the Department of Health (DOH) before introduce the GM foods into market. This document also provides guidance for food manufacturer, food trader, and health authorities as well, to evaluate safety of the GM foods and the producing process.

III. Definitions

1. Gene Modification Techniques

Techniques that apply genetic engineering or modern biotechnology to transfer or insert genetic material into a living cell or organism to result in genetic modification of the cell or organism. The technique does not include conventional breeding, cell fusion, protoplast fusion, hybridization, induced mutagenesis, *ex vivo* fertilization, somatic mutation, and polyploidy induction.

2. Genetically modified foods (GM foods)
Foods and food additives that are produced or manufactured from raw materials consisting or containing of GMOs.

3. Genetically Modified Organism (GMO)
An organism with genetic material that has been altered by gene modification techniques.

4. Host
An organism to which gene(s) or DNA fragment(s) are inserted or transferred by gene modification techniques

5. Vector
An agent that is used to deliver selected foreign DNA into host for proliferation and expression.

6. Transferred (or transgenic) or inserted gene (or DNA fragment)
Any foreign gene (or DNA fragment) that is transferred or inserted into host.

7. Gene products
Any product derived from the transferred or inserted gene(s) (or DNA fragment(s)).

8. Gene or DNA fragment donor
An organism that provides gene(s) or DNA fragment(s) for gene modification process.

IV. Scope

This guidance applies to GM foods that will be evaluated scientifically based on the concept of substantial equivalence and the following data (items 1~4) shall be scrutinized to determine the safety of GM foods for human consumption.

1. Information on the genetic materials.
2. Background information on history of human consumption.

3. Information on the food components.
4. Information on the difference in use between the new variety and its conventional counterpart.

Chapter Two: Safety Assessment of the Process of Producing GM Foods

This chapter describes safety assessment of the process of producing the GM foods that are not consumed directly. The manufacture methods, raw materials, equipment, apparatus, and refinement process used to produce GMO are evaluated as follows.

I. Methods of GMO production

The research and development of GMO in Taiwan shall observe the "Guidelines for experiments based on recombinant DNA techniques" of the National Science Council, "Guidelines for contained field trials of transgenic plants" and "Guidelines for contained field trials of transgenic animals" of the Council of Agriculture, and observe appropriate regulations promulgated by other government agencies. Information required for safety assessment of GMO are listed in Annex I or Annex II.

II. Non-GM raw materials and equipment for GM food production

Safety assessment is based on the following information:

A. History of raw materials or equipment that are used to manufacture food products or food additives

B. Safety of raw materials or equipment that are used to manufacture food products or food additives, or the experimental results of the following studies:

a. Acute toxicity
b. Sub-acute toxicity
c. Chronic toxicity
d. Reproductive effects
e. Mutagenic effects
f. Carcinogenic effects
g. Other necessary studies (e.g. intestinal tract toxicity, etc.)

All of the above studies should be conducted in facilities complying with Good Laboratory Practices. In some cases, certain of the above studies may be disregarded if the circumstance warrants the omission.

III. Refinement of Products

Food safety of the refined products will be assessed in accordance to the refinement methods used and the effects of the refinement process.

Chapter Three Safety Assessment of GM Foods

Safety assessment of GM foods is conducted toward organism(s) altered by gene modification techniques. Items to be evaluated are dependent on whether the GMO is directly consumed or not.

I. Safety assessment of the GMO that is not for direct human consumption**.**

A. Safety assessment of the GMO that is not directly consumed is conducted according to the following information:

a. Information of the GMO (for details see Annex I)
b. Document to certify that the product does not contain GMO.
c. Safety of substance(s) derived by using gene modification techniques.
d. Refinement process of the product.
e. Possible harmful effects caused by change in the contents or main ingredients of the GMO.

B. Additional information of the following studies for further evaluation shall be required if the decision based on the above information is inconclusive.

a. Acute toxicity
b. Sub-acute toxicity
c. Chronic toxicity
d. Reproductive effects
e. Mutagenic effects
f. Carcinogenic effects
g. Other necessary studies (e.g. intestinal tract toxicity, etc.)

All of the above studies should be conducted in facilities complying with Good Laboratory Practices. In some cases, certain of the above studies may be disregarded if the circumstance warrants the omission.

II. Safety assessment of the GMO that is for direct human consumption.

A. Safety assessment of GMO that is directly consumed is conducted according to the following information:

a. Information of the GMO (for details see Annex II)
b. Document to certify that the GMO consumed does not contain antibiotic marker gene (if antibiotic marker gene is found, evaluation is conducted according to Annex III.)
c. Allergenicity of the GMO, conducted according to Annex IV.
d. Information regarding to the safety of substance(s) derived by using Gene Modification Techniques
e. Refinement process of the product.
f. Any intended or unintended adverse effect to human health due to the alteration of the nutrient component in GMO.

B. Additional information on the following studies for further evaluation shall be required if the decision based on the above information is inconclusive.

a. Acute toxicity
b. Sub-acute toxicity

c. Chronic toxicity
d. Reproductive effects
e. Mutagenic effects
f. Carcinogenic effects
g. Other necessary studies (e.g. intestinal tract toxicity, etc.)

All of the above studies should be conducted in facilities complying with Good Laboratory Practices. In some cases, certain of the above studies may be disregarded if the circumstance warrants the omission.

Annex I - Information required to apply for the safety assessment of GMO that is not for direct human consumption

I. Application materials must include the following information:

A. Objective and usage of the GMO

B. Host

a. Taxonomy (scientific name, strain name, etc.)
b. Pathogenicity of the host organism and production of harmful physiologically active substances to demonstrate that the host is not pathogenic.
c. Capacity of becoming parasitic and striking root.
d. Information on foreign pathogenic factors (e.g. virus) to demonstrate that the host is free from contamination.
e. Survivability and reproducibility under simulated natural environments.
f. Biology of reproduction and its cross-breeding behavior.
g. The history of use as food.
h. Restrictive conditions on survival and proliferation abilities.
i. Pathogenicity and production of harmful physiologically active substance(s) of closely related species to the host.

C. Vector

a. Name
b. Origin
c. Properties or characteristics: 1. DNA size; 2. Restriction enzyme map; 3. Presence of any potentially harmful DNA sequence.
d. Drug resistance
e. Transmissibility
f. Host dependency
g. Method to construct the expression vector
h. Insertion method and site of the expression vector insertion

D. Transferred or inserted gene(s) (or DNA fragment(s))

a. Donor of gene(s) or DNA fragment(s)

1. Name and classification
b. Transferred or inserted gene(s) or DNA fragment(s)
1. Structure
1) Presence of DNA sequence to encode known toxic substance(s) or to produce hazard to human health.
2. Characteristics
1) Function
2) Restriction enzyme map
3) DNA size

E. GMO

a. New characteristics (properties) derived from gene modification techniques to demonstrate that it is not pathogenic.
b. Survivability and reproducibility under natural environment
c. Restriction on survival and reproduction[*1]
d. Method(s) of inactivation
e. Comparison between GMO and its host to demonstrate that it is not pathogenic and that it does not produce harmful physiologically active substance(s).

[*1] For industry use, the GMO should have same degree of safety as that of host, exhibiting only limited reproducibility under natural environment and no harmful effect on environment.

II. Literature and references

1. Documentation regarding the approval and consumption of the GMO in other countries.

2.Any other information to demonstrate safety of the GMO as food.

Annex II - Information on the safety assessment of GMO that is for direct human consumption

I. Application materials must provide the following information:

A. Objective and use of GMO

B. Host

a. Classification (scientific name, cultivar, systematic name, etc.)
b. Information on the genetically closely related species
c. Harmful physiologically active substance(s) produced
d. Allergenicity
e. Capacity of becoming parasitic and striking root
f. Information on foreign pathogenic factors (e.g. virus) to demonstrate that the host is free from contamination.
g. Survivability and reproducibility under simulated natural environments
h. Biology of reproduction and its cross-breeding behavior
i. The history of use as food

j. Safety of human consumption
k. Restrictive conditions on survival and proliferation abilities
l. Pathogenicity and production of harmful physiologically active substance(s) of related species to the host.

C. Vector

a. Name
b. Origin
c. Properties or characteristics
1. DNA size; 2. Restriction enzyme map; 3. Presence of any potentially harmful DNA sequence.
d. Drug resistance
e. Transmissibility
f. Host dependency
g. Method to construct the expression vector
h. Insertion method and site of the expression vector insertion.

D. Transferred or inserted gene(s) (or DNA fragment(s))

a. Donor of gene(s) or DNA fragment(s)
a) Name, origin, and classification
b) Safety of human consumption

E. Transferred or inserted gene(s) or DNA fragment(s)

a) Structure
1. Promoter
2. Terminator
3. Open Reading Frame
4. Presence of any potentially harmful DNA sequence
5. Other DNA sequence(s) known to affect gene expression

b) Characteristics
1. Function(s)
2. Restriction enzyme map
3. DNA size

c) Purity
d) Stability*1
e) Copy Number *1
f) Location, time and level of expression*[1]
g) Safety of the antibiotic-resistant marker gene*[1]
h) Transcription, expression, and possible product of the open reading frame*[1]

F. GMO

New characteristics (properties) derived from Gene Modification Techniques
b. Allergenicity of the transgene product(s)

c. Toxic effects of the transgene product(s)
d. Effects of the transgene products(s) on metabolic pathway*[2]
e. Nutrients and anti-nutrient, and any harmful effects caused by the altered substance(s)
f. Survivability and reproducibility under simulated natural environments
g. Restrictiive conditions and survival and proliferation abilities
h. Method(s) of inactivation
i. Method(s) of production, breeding and cultivation
j. Method(s) of production and management of the GMO seed

*[1] Also considers the possible changes that may occur within the GMOs.
*[2] Prepare information on the possible interactions between transgene product(s) and substances within the host.

II. Literature and references

1. Documentation regarding the approval and human consumption of the GMO in other countries
2. Any other information to demonstrate safety of the GMO as food

Annex III - Safety assessment of antibiotic-resistant marker gene

1. Information on antibiotic-resistant marker gene and gene products
1) Structure and function(s)
2) Mechanism of drug resistance, usage and related metabolic products
3) Methods of analysis and quantification
4) Changes resulted from preparing or processing
5) Changes in the digestive tract

2. Consumption of marker gene and its gene product
1) Estimated consumption amount
2) The use of the antibiotics targeted by the marker gene
3) Comparison of the marker gene with that of the gene in existing drug-resistance microbial strain
4) Estimated degree of inactivation of the antibiotics after oral administration and its possible problems

Annex IV - Application materials of safety assessment on allergenicity

1. The history for human consumption of the donor of the transgene(s)
2. Allergenicity of the transgene product(s)
3. Sensitivity of the transgene product(s) against physical and/or chemical treatment*[1]
4. Any apparent change of consumers caused by consumption of the transgene product(s)
5. Structure similarity of the transgene product(s) to any known food allergen
6. Percentage of the transgene product(s) in daily consumption of total proteins

Notes:

1) In some cases, certain of the above studies may be disregarded if the circumstance warrants the omission.

2) Additional information on the following studies for further evaluation shall be required if the decision based on the above information is inconclusive.
(1) Information on binding capacity between the transgene product(s) and the patient's IgE antibody which are induced by the allergen(s) that has structure similarity to the transgene product(s)
(2) Information on binding capacity between the transgene product(s) and the IgE antibody which are induced by patient's major allergens[*2*3]

[*1]Information on the sensitivity of the transgene product(s) in simulated gastric fluid, simulated intestinal fluid and under heat treatment (analyzed by SDS-PAGE and Western blot).

[*2]Analysis of Western blot and ELISA in evaluating the binding capacity between patient IgE antibody and the transgene product.

[*3]Analysis of the sera from patients who are known allergic to egg, milk, soybean, rice, wheat or buckwheat.

End text